Can information on functional and cognitive status improve short-term mortality risk prediction among community-dwelling older persons? A cohort study using a UK primary care database

Running header: Frailty predicts mortality in elderly

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Abstract

Background: Functional and cognitive domains have rarely been evaluated for their prognostic value in general practice (GP) databases. The aim of this study was to identify functional and cognitive domains in The Health Improvement Network (THIN) and to evaluate their additional value for the prediction of one-month and one-year mortality in elderly persons.
Methods: A cohort study was conducted in a UK nationwide GP database. A total of 1,193,268 patients ≥65 years, of whom 15,300 persons had dementia, were identified from 2000-2012. Information on mobility, dressing and accommodation was recorded in THIN frequently enough to be analyzed further. Cognition data could not be used due to very poor recording of data in THIN. One-year and one-month mortality was predicted using logistic models containing the variables age, sex, a disease score and functionality status.
Results: A significant but moderate improvement on one-year and one-month mortality prediction in elderly people was observed by adding accommodation to the variables age, sex and disease score, as the c-statistic (95%CI) increased from 0.71 (0.70-0.72) to 0.76 (0.75-0.77) and 0.73 (0.71-0.75) to 0.79 (0.77-0.80), respectively. A less notable improvement in the prediction of one-year and one-month mortality was observed in persons with dementia.
Conclusions: Functional domains moderately improved the accuracy of a model including age, sex and co-morbidities in predicting one-year and one-year mortality risk among community-dwelling older people, but were much less able to predict mortality in persons with dementia. Cognition could not be explored as a predictor of mortality due to insufficient data being recorded.

Keywords: elderly, frailty, database, mortality

1. Background

The last two decades have seen a significant increase in the number of observational studies investigating drug safety using electronic healthcare databases, particularly in elderly populations. Mortality is a widely explored outcome in such pharmacoepidemiological studies[1]. However, the data sources used to carry out such studies usually capture information that is limited to demographic information, medical history (diagnoses, laboratory results and medical procedures) and drug prescribing[2]. As a result, pharmacoepidemiological studies investigating the risk of death and other outcomes associated with drug use may suffer from residual unmeasured confounding due to frailty, if this remains unmeasured and unaccounted for in analyses. To date, there is no gold standard method of measuring frailty, however it may be defined, although a recent review suggests that a frailty index consisting of co-morbidities and healthcare claims which are indicative of frailty may be the best approach towards adjusting risk estimates in observational studies based on claims data[2].

In clinical practice, the two most commonly used models of frailty are: i) the phenotype model, defined by unintended weight loss, fatigue, general weakness, reduced walking speed and limited physical activity[3], and ii) the cumulative deficit model, defined by co-morbidities and impaired functionality or disability[4]. Although a recently published study proposed a composite 'frailty' score for primary care databases containing disease and non-disease indicators of health[5,6], the value of individual non-disease indicators of frailty as predictors of mortality in such resources remains unknown.

The aim of this study was therefore to investigate, using a large primary care database: (1) how frequently data on cognitive and functionality status is recorded in elderly community-dwelling persons and (2) the extent to which cognitive and functional status improve the prediction of mortality beyond commonly used covariates such as age, gender and co-morbidities.

2. Materials and methods

2.1 Data source and study population

The THIN database was used to carry the study. THIN contains electronic patient data recorded by general practitioners (GPs) during routine clinical practice and currently has anonymized clinical data for 11 million persons (covering approximately 6.2% of the UK population) registered with 562 general practices across UK. Demographic data in THIN is found in a patient file containing patient date of birth, date of death where applicable, sex, date of registration within the database and registration status within the database (i.e. whether the patient is active or has been transferred out of the database). All persons in the database have a unique and de-identified code which is used to link the patient file with other files such as the medical file. The medical file contains medical diagnoses, related information such as information on functional and cognitive domains, and the date when this information was recorded. Data on medical diagnoses in the medical file is coded using Read codes, the standard clinical terminology system that is used in general practice in the UK. THIN also has a prescription file which contains data on prescribed drugs such as the date of prescription, the generic name, the strength, and the formulation of the prescribed drug. Drug information is coded through British National Formulary (BNF) and Multilex codes.

Within THIN a cohort of persons aged 65 years and over, as well as a sub-cohort of persons in this age range having a dementia diagnosis was identified. Patients in the cohort of elderly persons were included in the study if they were aged 65 and over with at least one year of database history. The study period started from 1st January 2000 to 31st December 2012. The cohort entry date was therefore the date at which one year of database history was accumulated, the date at which persons had 65 years of age or the 1st January 2000, whichever came last.

2.2 Demographics and clinical history

Demographic characteristics (age and sex) were evaluated at the cohort entry date while clinical characteristics were evaluated any time prior to the cohort entry date. The co-morbidities chosen to describe the health status of the study population consisted of fifteen diseases that are part of the Quality and Outcomes Framework (QOF) program, a voluntary scheme available to all GPs in the UK which incentivizes GPs to register certain diseases[5]: asthma, atrial fibrillation, cancer (excluding non-melanotic skin cancer), chronic kidney disease stages 3-5, chronic obstructive pulmonary disease, coronary heart disease, dementia, depression, diabetes, epilepsy, heart failure, hypertension, hypothyroidism, psychosis, schizophrenia, bipolar disorders and stroke/transient ischaemic attack. However, the disease score employed in the present study consists of only nine out of the fifteen QOF diseases that were found to be predictive of mortality with a hazard ratio of 1.2 or higher (i.e., the standard QOF score) according to the original paper by Carey et al[5]. The following weights were applied to each of the nine QOF disease based on the size of the hazard ratio, thus quantifying the association between that disease and mortality in elderly persons: atrial fibrillation assigned one point; cancer assigned three points; chronic obstructive pulmonary disease assigned two points; dementia assigned three points; diabetes assigned one point; epilepsy assigned two points; heart failure assigned two points; psychosis, schizophrenia and bipolar disease assigned two points; stroke or transient ischaemic attack assigned one point. These diseases were identified in THIN using Read codes (see **Appendix A**).

2.3 Functional and cognitive domains

The THIN medical file was searched for Read codes related to the following functional/cognitive domains as identified in a comprehensive geriatric assessment chart previously used in geriatric epidemiological research[7,8]: nursing home resident or otherwise, activities of daily living (bathing, cooking, dressing, feeding, house-cleaning, money management, personal hygiene and toileting), nursing needs (bladder or bowel incontinence, nasogastric tube or other feeding tube, nephrostomy, long-term oxygen treatment, tracheostomy and urinary catheter), the presence of pressure sores, independence in mobility and cognitive decline. Once the most frequently recorded functional and cognitive codes were identified, these were grouped into functional/cognitive domains, i.e., umbrella terms for a particular aspect of functional/cognitive ability such as mobility (see **Appendix B**). Functional and cognitive domains were categorized into two or more levels to allow the identification of patients who are frailer than others, thus accounting for severity. For example, a functional/cognitive domain level would be given a value of 0 if it indicated good mobility and 1 if it indicated poor mobility (see **Appendix C**).

The proportion of functional and cognitive domains identified in THIN was calculated by dividing the number of patients with at least one relevant code recorded in the medical file from 2000 to 2012 by the number of eligible patients during the study period. This was done in order to identify which functional and cognitive domains were recorded frequently enough to be included in the mortality prediction (arbitrarily defined as a threshold of at least 5,000 persons based on preliminary patient frequencies).

For the cohort of elderly persons as well as persons with dementia having a recorded functional and cognitive domain, the index date was assigned as the date when subjects had a first recorded functional/cognitive domain. Aage and co-morbidities were re-evaluated at this date.

2.4 Statistical analysis

Demographic and clinical characteristics were reported as mean ± standard deviation (SD) or median (inter-quartile range) and frequency (percentage) for continuous and categorical variables, respectively.

The crude mortality rates within one year of follow-up (events per 100 person-years) and the crude mortality rates within one month of follow-up (events per 100 person-months)after the first-recorded functional/cognitive domains were calculated starting from the index date for all persons aged 65 and over and those with dementia separately. This was done by dividing the number of deaths by the number of person-years or person-months at risk, and multiplying this by 100.

Multivariable logistic models were fitted to predict one-year and one-month mortality risk and were applied to: 1) all patients and 2) patient subgroups within each functional/cognitive domain. When considering all patients, the discriminatory ability (i.e., the ability to distinguish subjects who will die from those who will not) achieved by a model, which included patient's age and sex only (model 1) was evaluated and compared to the discriminatory ability achieved by a new model additionally including the QOF co-morbidity score (model 2). When considering patient subgroups, the discriminatory ability of the model which included patient's age, sex and QOF co-morbidity score was compared to that achieved by a new model which further included the functional and cognitive domains (model 3).

The discriminatory ability achieved by each model was assessed by computing the area under the Receiver Operating Characteristics (ROC) curve (AUC; also known as the "c-statistic") along with its 95% confidence interval (95%CI)[9]. Comparisons between the c-statistics estimated from different models were performed following the DeLong method[10], and improvement in discriminatory ability was further evaluated by the Integrated Discrimination Improvement (IDI)[11]. In comparing the models, the IDI measures the increment in the predicted probabilities for the subset developing the event and the decrement for the subset not developing the event. It can also be interpreted as the change in R-squared coefficient obtained by adding the new covariate to the model (the magnitude of this change depends on the discriminatory ability provided by the model without the covariate). Moreover, the calibration of the models was evaluated. Calibration reflects the extent to which the predicted probabilities and actual probabilities agree and two well-known statistics were estimated: the calibration-in-the-large and the calibration slope[12]. The calibration can be characterized by an intercept, which indicates the extent that predictions are systematically too low or too high ('calibration-in-the-large'), and a calibration slope, which should be 1[13]

A two-sided p-value <0.05 was considered for statistical significance. All data management and statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

2.5 Subgroup and sensitivity analysis

The multivariable logistic models were stratified by gender in order to see whether mortality prediction differed between males and females. Moreover, in order to evaluate the presence of a potential selective registration of the functional/cognitive domains, mortality rates and Kaplan-Meier curves were estimated within one year of follow-up among persons aged 65 and over in THIN with and without a functional/cognitive domain recorded, irrespective of functional/cognitive domain severity.

3. Results

3.1 Cohort characteristics

From 2000 to 2012, 1,193,268 people aged 65 years or over were identified in THIN. The mean (SD) age of this study population was 70.7 (6.8) years and 55% were male (see **Appendix D**). The dementia cohort included 15,300 persons of whom 65% were males, with a mean (SD) age of 79.3 (6.2) years. The overall median survival time of the full cohort (survival from the cohort entry date until their date of death) was 5.5 years (inter-quartile range: 2.5-9.9), while this was lower in persons with dementia at 1.8 years (inter-quartile range: 0.8-3.5)). ,

Within one year of follow-up, the crude mortality rate among all persons aged 65 and over was 3.0 per 100 person-years (34,337 deaths observed in 1,138,128 person-years), while the crude mortality rate estimated within one month of follow-up was 0.3 per 100 person-months (3,166 deaths observed in 1,189,315 person-months). Among persons with a dementia diagnosis, the crude mortality rate at one year of follow-up was 13.0 per 100 person-years (1,656 deaths observed in 12,778 person-years) while the crude mortality rate within one month of follow-up was 1.1 per 100 person-months (171 deaths observed in 15,083 person-months).

3.2 Functional and cognitive domains

After the functional and cognitive domains found in THIN were defined, it was found that mobility (4.6%), accommodation (2.0%) and dressing ability (0.4%) were the most commonly recorded, each exceeding a threshold of 5,000 persons with a recorded code (**Table 1**), therefore only these domains were used to evaluate improvement in model's prognostic ability. The mobility domain was a two-level variable (i.e. 0=good mobility, 1=poor mobility), accommodation was a three-level variable (i.e. 0=lives with relatives or not alone, 1=lives alone in non-institutional accommodation, 2=lives in nursing home or other institutional accommodation), and dressing ability was a two-level variable (i.e. 0=independent, 1=dependent). As shown in **Appendix E**, all of three domains were recorded for only 217 (0.02%) persons.

3.3 Prediction of one-year and one-month mortality in elderly persons

Compared to the model based on age and sex only, the inclusion of the QOF co-morbidity score significantly improved the model's prediction accuracy of one-year mortality in patients $\geq$65, with the c-statistic increasing from 0.78 (95%CI: 0.78-0.79) to 0.82 (0.81-0.82) (p-value: <0.001) (**Table 2**). All functional domains statistically improved the discriminatory power of the models. Compared to age, sex and QOF co-morbidity score, the greatest improvement in prediction accuracy was found for accommodation, as shown by an increase in c-statistic from 0.71 (0.70-0.72) to 0.76 (0.75-0.77) (p-value: <0.001) as well as by a higher IDI, at 0.036 (0.033-0.039) (p-value: <0.001). Overall, the functional domains predicted one-month mortality slightly better than one-year mortality in the wider cohort (**Table 3**). The models for all elderly persons were found to be highly calibrated based on the Calibration in the large[@] and Calibration in the slope[@] statistics (details in **Appendix F and G**).

3.4 Prediction of one-year and one-month mortality in elderly persons with dementia

In the sub-cohort with dementia, only accommodation statistically improved the model's prediction accuracy of one-year mortality, albeit very modestly, with the c-statistic increasing from 0.63 (0.59-0.67) to 0.64 (0.61-0.68) (p-value:0.015) and an IDI value of 0.0098 (0.005-0.015) (p-value: <0.001) (**Table 2**). The model's prediction accuracy in the dementia sub-cohort was relatively poor for one-month mortality, as indicated by the lack of improvement in model discrimination when the QOF co-morbidity score was added to age and sex as predictors (**Table 3**). Accommodation and mobility improved the one-month mortality prediction modestly in the dementia sub-cohort with c-statistics increasing from 0.67 (0.58-0.76) to 0.71 (0.63-0.79) and 0.67 (0.60-0.75) to 0.69 (0.61-0.76) respectively (p-value: <0.001 for both). The effect of dressing on the logistic models predicting one-month mortality in dementia patients could not be evaluated as there were too few patients (n=143) with data recorded for this domain and very low number of events (n=2). The models for all elderly persons with dementia were also found to be highly calibrated based on the Calibration in the large[@] and Calibration in the slope[@] statistics (details in **Appendix F and G**).

3.5 Subgroup and sensitivity analysis

The subgroup analyses showed that there was no major difference between mortality prediction at one-year and-one month for females and males in either the full cohort or the dementia cohort, despite high model calibration (**Appendix H and I**). *Post hoc* analyses aiming to shed light on potential selective recording of functional domains identified showed that having a recorded functional/cognitive domain (irrespective of severity) was associated with higher mortality rates than not having a functional/cognitive domain at all (**Appendix J and K**). This difference was most pronounced for mobility and accommodation and less so for dressing.

4. Discussion

4.1. Findings in context

The main finding from this study is that information on functional domains found in a large primary care database moderately improves the prediction mortality at one year, and to a lesser extent at one month in mortality in elderly persons, when included in a model in addition to age, sex and a co-morbidity (QOF) score. This finding suggests that electronic primary healthcare databases such as THIN have currently unused potential to provide a more global assessment of geriatric health status compared to the standard diagnostic and prescription data that is usually used in pharmacoepidemiology studies. In addition, functionality status may possibly be used to address residual confounding. A recent study was able to developed an electronic frailty index using proxies of frailty in THIN to identify persons with mild, moderate and severe frailty, taking into account of a range of deficits, including clinical signs, symptoms, diseases and disabilities. This frailty index is an important development for future research conducted in electronic healthcare databases, suggesting that such data sources should be explored for their potential to harness frailty-related data in elderly persons.

Accommodation was found to be the best predictor of mortality at one year among older persons more generally and those with dementia specifically, most likely because persons who live relatively independently or have social support are likely to be healthier overall than those who are institutionalized[14]. Based on our classification of severity for this domain, persons living with relatives or not alone were considered to have a lowest risk of death while those living in a nursing home were considered to have the highest risk of death. The assumption underlying this choice was that persons not living alone may have a greater social and medical support, leading to a potentially low degree of frailty, while persons in a nursing home are already a much frailer population and therefore may be at higher risk of death. The latter was shown to be true using THIN database[15]. Based on the performance of the age, sex and co-morbidity adjusted models, we can conclude that the findings support our reasoning. Due to the limited information available on the nature of the living arrangements, the classification system used was however very simple and did not reflect the actual variety of such arrangements, each of way may have a different implication for functionality[16].

Data on cognition, a domain with great potential for the identification of frailty, in particular in persons with dementia, was very poorly recorded in this database and as a result could not be used to predict mortality. In general, among persons with dementia the functional domains were much less powerful in predicting mortality compared to those in elderly persons overall. This is likely to be because a population with heterogeneous traits is a pre-requisite for the prediction analysis, whereas the presence of a dementia diagnosis could result in the selection of a population with more homogeneous health risks. As a result, future pharmacoepidemiological research restricting similar analyses solely to persons with dementia may be similarly subject to such limitations in the prediction of mortality. It may be worth exploring whether the functionality domains identified may have other applications.

As expected, the number of deaths was substantially reduced when considering a time window of one month, leading to a significant loss of statistical power. As a result, no reliable conclusions can be drawn regarding one-month mortality. Educational interventions to promote the systematic assessment and recording of data on functional status for elderly persons by GPs could improve the identification of frail patients, even within such short time-frames in general medical practice. This in turn could inform clinicians on which category of patients requires more cautious pharmacological management, thus optimizing the quality of care in clinical practice on a large scale. There are currently existing databases that contain systematically recorded frailty data. An example is the

Arianna database, a GP database in Caserta (Campania region, Italy) where data on functional status (using the Barthel scale or Barthel index), mobility, accommodation, comprehension of language, hearing and visual impairment and mental health (using the Short Portable Mental Status Questionnaire- SPMSQ) is recorded systematically by GPs for approximately 75% of persons aged 65 and over[17]. Another example is the systematic registration of results of the SPMSQ, the Barthel index and the Exton-Smith pressure sore scale, as well as nursing care requirements and social network support for all elderly persons requesting nursing home admission or home-based nursing assistance from the national healthcare system in Padova (Veneto region, Italy). This data is available in the Administrative Repository Database of the ULSS 16 in Padova[8].

4.2 Strengths and limitations

A primary strength of this study is its novelty in systematically searching a large primary care database containing 11 million persons for functional and cognitive domains and the evaluation of these indicators as predictors of mortality. The use of co-morbidities and functional domains that relate to impaired functionality is consistent with the cumulative deficit model of frailty[4], and currently developed electronic frailty index[6]. Given the close link between accommodation status (e.g., institutional care), disability (based on independence or otherwise in the two activities of daily living evaluated) and frailty, we consider the choice of these functional domains to be justified as proxies of frailty and potential risk factors for death. Indeed, these domains were shown to be clinically meaningful as components of a frailty score in predicting mortality in previous work from which the functional domains in the present study were derived[7,8,17]. A major strength of the present study is the use of the QOF co-morbidity score as a reference model when comparing the performance of the functional and cognitive domains, since the QOF co-morbidity score has been recently used and validated in a cohort of elderly persons identified in THIN, and found to predict mortality better than the Charlson co-morbidity score. The models themselves were thoroughly tested for discrimination and calibration. The present study also investigated the value of data on the severity of functional status in view of potential selective data recording in the prediction of mortality, while to our knowledge this has not been done before.

However, this study also has some limitations. The prevalence of selected diseases, including dementia, identified in THIN may be lower than expected. The reason for this is that data is recorded during routine medical practice and not for direct research purposes. This may affect the generalizability of the results but not the validity. The number of persons with at least functionality domain recorded was low, and is therefore unlikely to reflect the real proportion of functionality problems all elderly persons. The predictive accuracy of the logistic models used was contingent on the frequency of functional domain codes recorded in the database, which was found to be generally low. In addition, the discriminatory power of the models was limited by the relatively narrow range of risk factors, that is, age, sex andthe QOF morbidity score. While a greater variety and volume of functionality data would have improved the discrimination of the models, the present study highlights that the prediction of mortality is nevertheless improved moderately in older persons even using limited data on functional domains. The information available on functional domains itself was simple compared to the complexity and range of possible impairment, which we had to limit description to binary variables for mobility and dressing ability, and to 3 simple categories for accommodation. Although the impact of multiple functionality problems on risk of mortality in elderly persons is important, given that elderly persons may very well have more than one functionality impairment, it was not possible to study this due to the very low number of persons with more than one functionality problem. The QOF co-morbidity score did not improve mortality prediction as significantly in people with dementia, suggesting that factors other than those analyzed may have played a role in the

mortality risk among these patients. In fact, the inclusion of accommodation in the logistic models predicting mortality at one year and one month in persons with dementia moderately improved the prediction of mortality (compared to the model including age, sex and QOF morbidity score) more than the inclusion of the QOF morbidity score (compared to the model including only age and sex). Furthermore, post-hoc analysis showed that functionality variables were selectively recorded among persons who appeared to be at higher risk of death. While this reduces the generalizability of results to persons not having a functionality code recorded, the validity of the findings for persons with a functionality code recorded is not affected.

5. Conclusion

The limited data recorded on functionality domains in a large UK primary care database moderately improved the prediction of mortality in elderly persons, and were much less powerful when predicting mortality in persons with dementia. Data on cognition was recorded too poorly for this domain to be explored as a predictor of mortality. Such proxies of frailty may be of value in accounting for some unmeasured confounding in epidemiologic analyses, provided that the limitations of this data are well-understood.

Declarations

Ethics approval and consent to participate: The present study did not involve direct contact with human participants since all the data used was collected retrospectively during routine clinical practice. All patient-level data used was anonymized. The present study was part of a larger study approved by the EPIC Scientific Review Committee (SRC 13-085).

Competing interests: The authors declare that they have no conflict of interest related to the present paper.

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Authors' contributions: Conceived the paper- GT; Provided the data- GT, MS; Conducted data management- JS, FG; Conducted data analysis- AF; Wrote and/or critically revised the manuscript- JS, AF, FG, GB, EP, AP, MM, RS, MS, GT.

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Table 1: Most commonly registered functional domains in THIN among all patients aged 65 years or over.

Domains N (%)	**Category**	**N (%)**
Mobility N=55,597 (4.7%)	0=good mobility	3,540 (6.37%)
	1=poor mobility	52,057 (93.63%)
Accommodation N=23,684 (2.0%)	0=lives with relatives or not alone	6,485 (27.38%)
	1=lives alone in non-institutional accommodation	5,714 (24.13%)
	2=lives in nursing home or other institutional accommodation	11,485 (48.49%)
Dressing ability N=5,197 (0.4%)	0=independent	4,747 (91.34%)
	1=dependent	450 (8.66%)

Table 2: One-year mortality risk prediction in a cohort of patients aged 65 and over, and those with dementia in THIN.

Sample	Patient subgroups	Events / N° subjects (%)	Logistic model	C-statistic (95%CI)	p-value [a]	IDI (95%CI)	p-value [b]
Elderly	All patients	34,337/1,193,268 (2.9)	Age + Sex	0.78 (0.78-0.79)	---	[reference]	---
			Age + Sex + QOF score	0.82 (0.81-0.82)	<0.001	0.0151 (0.0145; 0.0158)	<0.001
	Patients with accommodation registration	3,764/23,684 (15.9)	Age + Sex + QOF score	0.71 (0.70-0.72)	---	[reference]	---
			Age + Sex + QOF score + Accommodation	0.76 (0.75-0.77)	<0.001	0.0360 (0.0333; 0.0387)	<0.001
	Patients with mobility registration	11,069/55,597 (19.9)	Age + Sex + QOF score	0.66 (0.65-0.66)	---	[reference]	---
			Age + Sex + QOF + Mobility	0.66 (0.66-0.67)	<0.001	0.0034 (0.0030; 0.0039)	<0.001
	Patients with dressing registration	379/5,197 (7.3)	Age + Sex + QOF score	0.70 (0.67-0.72)	---	[reference]	---
			Age + Sex + QOF score + Dressing	0.72 (0.70-0.75)	<0.001	0.0207 (0.0138; 0.0276)	<0.001
Elderly with dementia	All patients	1,656/15,300 (10.8)	Age + Sex	0.66 (0.64-0.67)	---	[reference]	---
			Age + Sex + QOF score	0.66 (0.65-0.69)	<0.001	0.0052 (0.0037; 0.0068)	<0.001
	Patients with accommodation registration	286/1,174 (24.4)	Age + Sex + QOF score	0.63 (0.59-0.67)	---	[reference]	---
			Age + Sex + QOF score + Accommodation	0.64 (0.61-0.68)	0.015	0.0098 (0.0051; 0.0146)	<0.001
	Patients with mobility registration	348/1,497 (23.2)	Age + Sex + QOF score	0.59 (0.55-0.62)	---	[reference]	---
			Age + Sex + QOF score + Mobility	0.59 (0.55-0.62)	0.592	0.0015 (-.00003; 0.0033)	0.051
	Patients with dressing registration	28/143 (19.6)	Age + Sex + QOF score	0.62 (0.51-0.73)	---	[reference]	---
			Age + Sex + QOF score + Dressing	0.69 (0.58-0.80)	0.134	0.0333 (0.0047; 0.0618)	0.011

[a] p-value from DeLong test for difference between the two c-statistics

[b] p-value from test that IDI is not significantly different than zero

Abbreviations: CI: confidence interval; IDI: Integrated Discrimination Improvement; QOF- quality outcomes framework score

Table 3: One-month mortality prediction in a cohort of patients aged 65 and over, and those with dementia in THIN.

Sample	Patient subgroups	Events / N° subjects (%)	Logistic model	C-statistic (95%CI)	p-value[a]	IDI (95%CI)	p-value[b]
Elderly	All patients	3,166/1,193,268 (0.3)	Age + Sex	0.78 (0.78-0.79)	---	[reference]	---
			Age + Sex + QOF score	0.83 (0.82-0.83)	<0.001	0.0028 (0.0025; 0.0031)	<0.001
	Patients with accommodation registration	503/23,684 (2.1)	Age + Sex + QOF score	0.73 (0.71-0.75)	---	[reference]	---
			Age + Sex + QOF score + Accommodation	0.79 (0.77-0.80)	<0.001	0.0091 (0.0078; 0.0103)	<0.001
	Patients with mobility registration	1,903/55,597 (3.4)	Age + Sex + QOF score	0.65 (0.63-0.66)	---	[reference]	---
			Age + Sex + QOF score + Mobility	0.66 (0.65-0.67)	<0.001	0.0015 (0.0013; 0.0017)	<0.001
	Patients with dressing registration	20/5,197(0.4)	Age + Sex + QOF score	0.77 (0.65-0.89)	---	[reference]	---
			Age + Sex + QOF score + Dressing	0.80 (0.68-0.92)	0.368	0.0139 (0.0005; 0.0273)	0.021
Elderly with dementia	All patients	171/15,300 (1.1)	Age + Sex	0.65 (0.60-0.69)	---	[reference]	---
			Age + Sex + QOF score	0.67 (0.63-0.72)	0.027	0.0015 (0.0004; 0.0027)	0.004
	Patients with accommodation registration	36/1,174(3.1)	Age + Sex + QOF score	0.67 (0.58-0.76)	---	[reference]	---
			Age + Sex + QOF score + Accommodation	0.71 (0.63-0.79)	<0.001	0.0052 (0.0037; 0.0066)	<0.001
	Patients with mobility registration	50/1,497(3.3)	Age + Sex + QOF score	0.67 (0.60-0.75)	---	[reference]	---
			Age + Sex + QOF score + Mobility	0.69 (0.61-0.76)	<0.001	0.0021 (0.0015; 0.0027)	<0.001

[a] p-value from DeLong test for difference between the two c-statistics

[b] p-value from test that IDI is not significantly different than zero

Abbreviations: CI: confidence interval; IDI: Integrated Discrimination Improvement; QOF- quality outcomes framework score